

## CLAIMS

1. A synthetic multivalent T cell receptor (TCR) complex for binding to a MHC-peptide complex, which TCR complex comprises a plurality of T cell receptors specific for the MHC-peptide complex.
- 5 2. The TCR complex according to claim 1, wherein the T cell receptors are  $\alpha\beta$  T cell receptors having an  $\alpha$  chain and a  $\beta$  chain.
3. The TCR complex according to claim 2, wherein the  $\alpha$  chain and  $\beta$  chain are soluble forms of T cell receptor  $\alpha$  and  $\beta$  chains.
- 10 4. The TCR complex according to any preceding claim, wherein the T cell receptors are in the form of multimers of two or more T cell receptors.
5. The TCR complex according to claim 4, wherein the multimer is a trimer or a tetramer.
6. The TCR complex according to any preceding claim, wherein the T cell receptors are associated with one another via a linker molecule.
- 15 7. The TCR complex according to claim 6, wherein the linker molecule is a multivalent attachment molecule such as avidin, streptavidin or extravidin.
8. The TCR complex according to claim 7, wherein at least one of the T cell receptor  $\alpha$  or  $\beta$  chains is derived from a fusion protein comprising an amino acid recognition sequence for a modifying enzyme such as biotin.
- 20 9. The TCR complex according to claim 8, wherein the T cell receptors are biotinylated.
10. The TCR complex according to any preceding claim, comprising a multimerised recombinant T cell receptor heterodimer having enhanced binding capability compared to a non-multimeric T cell receptor heterodimer.
- 25 11. A multivalent TCR complex comprising a multimerised recombinant T cell receptor heterodimer having enhanced binding capability compared to a non-multimeric T cell receptor heterodimer.
12. The TCR complex according to any preceding claim, wherein the T cell receptor is a refolded recombinant T cell receptor which comprises:
  - 30 i) a recombinant T cell receptor ( $\alpha$  or  $\gamma$  chain extracellular domain having a first heterologous C-terminal dimerisation peptide; and
  - ii) a recombinant T cell receptor  $\beta$  or  $\delta$  chain extracellular domain having a second C-terminal dimerisation peptide which is specifically

heterodimerised with the first dimerisation peptide to form a heterodimerisation domain.

13. The TCR complex according to claim 12, wherein a disulphide bond present in native T cell receptors between the  $\alpha$  and  $\beta$  or  $\gamma$  and  $\delta$  chains adjacent to the cytoplasmic domain, is absent from the recombinant T cell receptor.

14. The TCR complex according to claim 12 or claim 13, wherein the heterodimerisation domain is a coiled coil domain.

15. The TCR complex according to claim 14, wherein the dimerisation peptides are c-jun and c-fos dimerisation peptides.

16. The TCR complex according to any one of claims 12 to 15, comprising a flexible linker located between the T cell receptor chains and the heterodimerisation peptides.

17. The TCR complex according to any one of claims 10 to 16, wherein the T cell receptor is expressed in an E.coli expression system.

18. The TCR complex according to any one of claims 10 to 17, wherein the T cell receptor is biotinylated at the C-terminus.

19. The TCR complex according to any preceding claim, wherein the T cell receptors are associated with a lipid bilayer.

20. The TCR complex according to claim 19, wherein the lipid bilayer forms a vesicle.

21. The TCR complex according to claim 20, wherein the T cell receptors are attached at the exterior of the vesicle.

22. The TCR complex according to claim 20 or claim 21, wherein the T cell receptors are attached to the vesicle via derivatised lipid components of the vesicle.

23. The TCR complex according to claim 19 or claim 20, wherein the T cell receptors are embedded in the lipid bilayer.

24. The TCR complex according to any one of claims 1 to 18, wherein the T cell receptors are attached to a particle.

25. The TCR complex according to any preceding claim, further comprising a detectable label.

26. The TCR complex according to any preceding claim, further comprising a therapeutic agent such as a cytotoxic agent or an immunostimulating agent.

5 27. The TCR complex according to any preceding claim, in a pharmaceutically acceptable formulation for use *in vivo*.

28. A method for detecting MHC-peptide complexes which method comprises:

- 10 (i) providing (a) a synthetic multivalent T cell receptor complex comprising a plurality of T cell receptors, and/or (b) a synthetic multivalent T cell receptor complex comprising a multimerised recombinant T cell receptor heterodimer having enhanced binding capability compared to a non-multimeric T cell receptor heterodimer, said T cell receptors being specific for the MHC-peptide complexes;
- 15 (ii) contacting the multivalent TCR complex with the MHC-peptide complexes; and
- (iii) detecting binding of the multivalent TCR complex to the MHC-peptide complexes.

29. The method according to claim 28, wherein the multivalent TCR complex is provided with a detectable label.

20 30. The method according to claim 28 or claim 29, for detecting cells presenting a specific peptide antigen.

31. The method according to any one of claims 28 to 30, wherein the multivalent TCR complex is a multivalent TCR complex according to any one of claims 1 to 27.

25 32. A method for delivering a therapeutic agent to a target cell, which method comprises:

- 30 (i) providing (a) a synthetic multivalent TCR complex comprising a plurality of T cell receptors, and/or (b) a synthetic multivalent TCR complex comprising a multimerised recombinant T cell receptor heterodimer having enhanced binding capability compared to a non-multimeric T cell receptor heterodimer, said T cell receptors being specific for the MHC-peptide complexes and the multivalent TCR complex having the therapeutic agent associated therewith;
- 35 (ii) contacting the multivalent TCR complex with potential target cells under conditions to allow attachment of the T cell receptors to the target cell.

33. The method according to claim 32, wherein the multivalent TCR complex is a multivalent TCR complex according to any one of claims 1 to 27.